Stroke remains a serious medical and socioeconomic challenge. And its incidence is increasing - the number of ischemic stroke-related deaths will increase from 3.29 million in 2019 to 4.90 million in 2030. Approximately 70-80% of strokes are ischemic caused by cessation of cerebral blood flow. So far, the only therapeutic strategy is recanalization – pharmacological or mechanical. However, only a small proportion of patients can be treated these ways. There are no proven neuroprotective factors. The pathophysiology of ischemia-related brain damage is complex and comprise many elements with glutamate-related excitotoxicity, ionic imbalances, neuroinflammation, oxidative stress, etc. All these phenomena affect the structure and the function of the neurovascular unit (NVU), which is a functional complex present in the brain, formed by various cells (vascular, glial, neurons). The NVU is responsible for the maintenance of a highly selective blood–brain barrier (BBB) and cerebral homeostasis, as well as the control of cerebral blood flow. The dysregulation of several transporting systems at the NVU under ischemic conditions plays significant role in stroke pathophysiology. In addition, some of the stroke risk factors, such as hyperglycemia and diabetes mellitus affects negatively transporters function aggravating brain injury and worsening stroke outcome.

The volume-regulated anion channels (VRACs), which are ubiquitously expressed in mammalian cells, are activated by cell swelling or reactive oxygen species what result in efflux of glutamate, aspartate, or taurine, inter alia.

This project is aimed to determine the effects of VRACs inhibition on the NVU function under ischemic condition.

We will use an *in vivo* model of focal brain ischemia in rats. In order to investigate sex-related differences, we will include both male and female animals. In addition, we will study how diabetes affects the NVU function in ischemic brain.

We will analyze: neurological deficits, infarct volume, real-time neurotransmission and cell activity, several aspects of the NVU function, BBB integrity, expression of selected molecules on the mRNA and protein levels, extracellular changes in gliotransmitters levels.

We hope, that results of this project will provide data that will be useful not only for brain ischemia but also for other conditions, in which the NVU function, and/or VRACs play important roles.